Arguments/Remarks

Favorable consideration of this application is respectfully requested in view of the foregoing amendments and the following remarks. Claims 8-10 and 13-15 are pending in the application. Claims 8-10 and 13-15 have been rejected. Claim 14 has been cancelled. No new matter has been added.

Rejection Under 35 USC §103(a), Obviousness

Claims 8-10 and 13-15 are rejected under 35 U.S.C. §103(a), as being unpatentable over Billich (US patent 5,538,997)(hereafter, "Billich reference") in view of Häbich (US patent 5,633,231)(hereafter, "Häbich reference") and Scholz (D Scholz et al., J. Med. Chem. (1994) 37, 3079)(hereafter, "Scholz reference"). Specifically, the Examiner posits that Billich teaches the instantly claimed compound (example 11) where the only difference is the N-protecting group 3-methylbenzyl ester vs. the benzyl ester. Applicants disagree for at least the following reasons.

As the Examiner states, the compounds of Billich et al are contemplated as HIV inhibitors. In contrast to that, the compounds of the present invention have found to be useful for the treatment of a proliferative disease, e.g. of a solid tumor. Billich et al exemplifies 61 compounds, only **5** of which (Examples 4, 11, 21, 22 and 30) show the (non chiral) "2-hydroxybenzyl substituted in 4 position by methoxy" as residue R4. The vast majority of compounds (**49**) possess a 2(R)--hydroxyindan-1(S)-yl residue at position R4. The compounds with the (chiral) 2(R)--hydroxyindan-1(S)-yl residue at position R4 are the only claimed compounds.

Scholz et al, J.Med.Chem 1994, 37, 3079-3089 also teaches compounds as HIV inhibitors. In contrast to that the compounds of the present invention have found to be useful for the treatment of a proliferative disease, e.g. of a solid tumor. Scholz et al determined, that replacement of the aminobenzyl group (substituent R, general structure of table 5) by a benzimidazoyl moiety leads to a 4 times more potent compound ("major increase in potency") (compound 44 vs 6), (Page 3083, table 5 and discussion). The benzimidazoyl moiety is also present in the most active compound 50.

The teachings of Scholz combined with Billich therefore teach one of skill in the art away from (simpler) benzyl derivatives towards bicyclic moieties which are either chiral or heterocyclic, particularly for treatment of HIV, which the references disclose. It is a surprising discovery therefore, that compounds bearing "2-hydroxybenzyl substituted in 4 position by

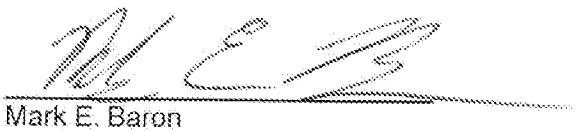
methoxy" as residue R4 are favorable for the treatment of proliferative diseases. When viewing the prior art as a whole, this is an unobvious alteration therefrom.

Applicants respectfully request entry of the amendments to the claims and the specification and submit no new matter is added thereby. Should the Examiner have any questions, please contact the undersigned attorney.

However, if it is deemed that additional fees are required, the Commissioner is authorized to charge Deposit Account No. 504409 in the name of Novartis for any fees due.

In view of the above, an early Notice of Allowance is respectfully requested.

Respectfully submitted,



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